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(54) Abstract Title

**Treatment of acne vulgaris skin condition by irradiation with light of specific wavelengths to target specific chromophores & stimulate collagen production**

(57) There is provided apparatus for the cosmetic treatment of a skin condition which comprises means for delivering illuminating radiation to a target skin zone or structure.

The skin condition may be acne vulgaris or Rosacea.

A method for the treatment of such a skin condition comprises directing illuminating radiation (including that of a predetermined wavelength) to a target skin zone in accordance with a predetermined delivery regime in order to effect (preferably contemporaneously) at that zone:

(a) a reaction which leads to at least partial disabling or eradication of the cause of the skin condition and

(b) non-ablative heating of the tissue in order to stimulate an inflammatory response to a degree sufficient to effect collagen production.

The illuminating radiation may be delivered continuously or in pulse mode (eg with pulses in the range 10  $\mu$ s to 100 ms, especially 50  $\mu$ s to 10 ms) and its source may comprise laser diodes or light emitting diodes (LED's), with filters for the required selected wavelength, if necessary.

The wavelength of the illuminating radiation is preferably in the range 400-1500 nm, especially 500-650 nm and preferably comprises a narrow wavelength band in the range 570-595 nm (yellow). The energy density is preferably in the range 0.5-5 J/cm<sup>2</sup>, with the apparatus advantageously being configured to allow variable selection of energy densities within that range but inhibit output above that range.

For acne vulgaris, interaction (a) above is achieved by targeting the chromophore porphyrin in haemoglobin which aggregates at the site of inflammation. Excitation with yellow light (ca 585 nm) produces singlet oxygen photochemically which destroys the adjacent bacterium responsible for acne vulgaris (propionibacterium).

Interaction (b) above is achieved by targeting the chromophore (oxy)haemoglobin in the dermal vasculature. The resulting photothermolysis effect stimulates, via inflammatory mediators, the production of fibroblasts which are responsible for the production of collagen, the skin's natural filling material, which improves skin texture and appearance.

Cosmetic Treatment Of Skin Conditions

The present invention relates to cosmetic treatment of skin conditions such as, for example, Acne Vulgaris.

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Acne Vulgaris is a condition of the sebaceous glands which affects 80% of individuals between the ages of 11 and 30. It is not confined to these age groups however and can affect all ages from neonates to the elderly. Factors which are considered of primary significance to the condition include an increase in the production of sebum, abnormal follicular keratinisation, the presence of Propionibacterium and subsequent inflammation.

15 Dependant on the size, content, and depth of the inflamed acne lesion, it is defined as a papule (less than 0.5cms in diameter), nodule (elevated solid lesion > than 0.5cms) pustule (a papule what contains purulent material) or a cyst (nodule that contains fluid or semisolid matter).

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Hair follicles are minute passages in the skin, which allow hairs to grow and produce sebum secretions from sebaceous glands which are housed within the hair follicle. Due to increased androgen levels or an excessive reaction by the sebaceous glands to androgen production, the sebaceous glands enlarge resulting in increased secretion of sebum which along with the keratinisation process of the epithelial cells, clog the hair follicle. Initially these blockages are microscopic then develop into whiteheads or blackheads (Comedones). Congested follicles are an ideal medium for growth of bacteria. When sebum levels are

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increased, the skin commensal propionibacterium ingest the clogged sebum under the skin and chemicals are produced which trigger the immune system to initiate the inflammatory changes and erythematous macules associated  
5 with Acne Vulgaris.

Inflammation is the body's response to invasion of pathogens and the redness associated with the acne lesions is the result of increased blood flow whereby the white  
10 blood cells invade bacterial cells and damage tissue and produce pus. Other fluids flood to the area and collect at the site of the inflamed tissue. ---

The approaches which are currently used for tackling Acne  
15 Vulgaris include Drug therapies (Systemic antibiotics, cortisone injections, Dianette (women only contraceptive pill, Roaccutane, Retinoids), PUVA (Psoralen and Ultra Violet light, type A), UVB Phototherapy, Dermalux (a system using a combination of red and blue light to treat acne),  
20 Peeling agents, laser resurfacing, Dermabrasion and Microdermabrasion.

According to the present invention, there is provided a method for the cosmetic treatment of a skin condition  
25 (particularly acne vulgaris), the method comprising directing illuminating radiation, including illuminating radiation of a predetermined wavelength, toward a target zone of skin in accordance with predetermined delivery regime in order to effect at the target zone a plurality  
30 of interactions, including:

- a) a reaction leading to at least partial disabling or eradication of the cause of the skin condition; and,
- 5        b) non-ablative heating of tissue stimulating an inflammatory response to a degree sufficient to effect collagen production.

The two-fold interaction system effected by the  
10 illuminating radiation provides an extremely effective cosmetic effect in that the interaction acts to clear up the skin condition and also stimulates the production of collagen to improve skin appearance (minimizing the appearance of scarring caused by the condition). A feature  
15 of the technique of the invention is that efficacy is achieved without the need of any other topically applied agent or any invasive or ablative procedure.

It is preferred that the interactions a) and b) defined  
20 above occur substantially contemporaneously.

The radiation is typically low intensity (avoiding ablation at or below the skin surface) and typically primarily of wavelength at or about the wavelength of yellow light  
25 (585nm) for reasons explained in detail later. Absorption of light is through the dermal vasculature having no adverse effects on the epidermis.

Desirably, the reaction leading to at least partial removal  
30 or disabling of the cause of the skin condition is a photochemical reaction.

Beneficially, the heating interaction is a photothermal effect caused by selective absorption of the predetermined wavelength light, typically by a preselected chromophore.

5 For Acne Vulgaris the chromophore targeted to combat the  
propionibacterium is porphyrin in the connective tissue.  
This tissue bound photosensitizer when excited from light  
of a certain wavelength (approximately the wavelength of  
yellow light - 585nm), produces a photochemical reaction  
10 resulting in the production of singlet oxygen thereby  
destroying the bacterium.

Propionibacterium is averse to oxygen (anaerobic) and  
relies upon chemicals known as porphyrins in skin tissue.  
15 Porphyrin is usually innocuous in the absence of light. It  
is however photosensitive and when exposed to light of the  
required wavelength the photochemical reaction occurs.  
This results in a transition from the porphyrin's ground  
state to a reactive triplet state. At this level, a  
20 reaction with molecular oxygen creates singlet oxygen.  
Through the medium of a suitable light source, to activate  
the porphyrins to produce singlet oxygen, the bacterium  
responsible for Acne Vulgaris can be cleared in a cosmetic,  
pain-free, non-invasive and efficient manner.

25 Vasodilation and hyperemia are integral parts of the  
inflammatory response, including response to infection.  
Therefore any inflammatory/infective focus contains a  
disproportionate concentration of red blood cells.

30 Porphyrin molecules are contained in the hem of

haemoglobin so that any inflammatory or infective focus contains a concentration of natural porphyrin. Activation of this porphyrin using, for example, yellow (585nm) light releases substances which destroys adjacent toxins such as  
5 bacteria in acne.

Similarly, any acute inflammatory condition of skin such as rosacea will be helped although the exact toxin may be unknown.

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Secondly, targeting the chromophore haemoglobin in the dermal vasculature plexus to create thermal injury stimulates the production of fibroblasts which is responsible for collagen production. The stimulated  
15 collagen produced is the skin's natural filling material, which will cosmetically improve skin texture and appearance. Exposure to light (of a relevant selected wavelength) results in a selective, non-ablative photothermolysis effect in the target chromophore, that is  
20 oxyhaemoglobin. The interaction of the radiation (light) within the dermal vascular plexus induces an inflammatory/growth response. This results in the release of inflammatory mediators from the endothelial cells through the vessel walls and into the dermal interstitium  
25 where they stimulate fibroblast activity. Fibroblasts are quiescent unless stimulated by inflammatory mediators. This creates a response by the fibroblasts to initiate tissue repair mechanisms which will in turn produce enhanced new collagen which is the skin's natural filling  
30 material and will improve skin texture and appearance.

The energy density of the energy delivered should be accurately controlled and monitored so as not to exceed a predetermined threshold level.

- 5 In order to stimulate fibroblast activity, the incident light must be absorbed in the microvasculature to release the necessary mediators which trigger fibroblast activity and hence collagen production.
- 10 Certain wavelengths of above, for example, 600nm (for example, 660nm - red) are not optimum for collagen stimulation as red light is not preferentially absorbed in haemoglobin/oxyhaemoglobin. An alternative option is to use two wavelengths, one with a high absorption in
- 15 porphoryin, which has absorption peaks other than those in the yellow region, and at least one wavelength at yellow (570-590nm).

- Where the skin condition is Acne Vulgaris it is therefore
- 20 preferred that the wavelength of the illuminating radiation comprises a primary wavelength or narrow wavelength band substantially in the range 570-590nm.

- Beneficially the radiation delivered is pulsed, the pulse
- 25 duration preferably being less than the thermal relaxation time of the target structure. This limits and controls the thermal damage done to the target structure, and controls the correct thermal and chemical response as required.

- 30 The photochemical interaction is typically dependent upon the number of incident photons, so the photons may be

delivered in pulsed or continuous wave mode. However, for the stimulation of collagen, pulsed operation is preferred to ensure delivery of the required energy regime to cause the triggering of the release of inflammatory mediators.

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The light (radiation) source may comprise laser sources (such as laser diodes) or light emitting diodes (LED's) if necessary with appropriate filter(s) to promote propagation of the required selected wavelength (or narrow wavelength band).

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Also by using pulsed operation, light emitting devices (particularly LED's) may be driven harder to produce more light output. A typical LED can operate at a drive current of 50mA in continuous mode, whilst in pulsed operation, for short periods, the same diode can be pulsed at current of around 200mA. This pulsed operation may be between 1 $\mu$ s to 100msec (1 $\mu$ s to 5ms preferred). This will allow fewer diodes to be used for a given output power requirement or a larger area to be treated with same amount of diodes.

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The target for the light source has to be a material that absorbs a specific wavelength and disregards other wavelengths (chromophore). In accordance with the invention, for Acne Vulgaris, the chromophores may be porphyrin in skin tissue and oxyhaemoglobin in the dermal vasculature.

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The preferred wavelength (or wavelengths) for this invention will depend upon the skin condition being treated but typically include a wavelength in the range of 400nm to

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1500nm with a preferred range of 500-650nm. Energy density is in the range of  $0.5\text{-}5\text{J}/\text{cm}^2$  via a pulsed or continuous wave. For pulsed operation the range is  $10\mu\text{s}$  to 100ms with a preferred range of  $50\mu\text{s}$  to 10ms.

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According to a further aspect, the invention provides apparatus for cosmetic treatment of a skin condition (particularly Acne Vulgaris), the apparatus comprising illuminating radiation delivery means for delivering  
10 illuminating radiation to a target skin zone or structure.

The apparatus is preferably arranged to output radiation of a discrete wavelength (or narrow primary wavelength band) substantially in or about the range 400nm-1500nm, depending  
15 upon the skin condition being treated. For treatment of acne vulgaris the preferred range is 500nm-650nm, most preferably 570nm-595nm.

The apparatus preferably delivers radiation at an energy  
20 density at the skin surface substantially in the range  $0.5\text{J}/\text{cm}^2$  -  $5\text{J}/\text{cm}^2$ . The apparatus is preferably configured to inhibit output of energies substantially above this range. Desirably the apparatus is configured to permit variable selection of energy densities within the range.

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The illuminating radiation may be pulsed or continuous wave. Pulsed energy may be preferred in order to avoid overheating of the target tissue structure (describe above) and produce the appropriate inflammatory response for  
30 collagen production. Pulse duration is preferably substantially in the range 10 microseconds - 100ms

(preferably substantially in the range 50microseconds - 10ms).

According to a further aspect, there is provided a method  
5 for the manufacture of an agent for the treatment of a skin condition (particularly Acne Vulgaris), the agent comprising illuminating radiation active to effect at the target zone the following interactions:

- 10 a) a reaction leading to at least partial disabling of the cause of the skin condition; and,
- b) non-ablative heating of tissue stimulating an inflammatory response to a degree sufficient to  
15 effect collagen production.

The invention has been primarily described in relation to the cosmetic treatment of Acne Vulgaris. It will however be appreciated that the two-fold nature of the action  
20 described for the invention has potential with respect to other skin conditions, including for example acute inflammatory conditions such as Rosacea, depending upon the selection of the appropriate chromophore/toxin.

CLAIMS:

1. A non-surgical method for the cosmetic treatment of a skin condition comprising directing illuminating  
5 radiation toward a target zone of skin in accordance with predetermined delivery regime in order to effect at the target zone a plurality of interactions, including:
  - 10 (a) a reaction leading to at least partial disabling or eradication of the cause of the skin condition; and
  - (b) non-ablative heating of tissue stimulating an inflammatory response to a degree sufficient to effect collagen production.
- 15 2. A method according to claim 1, for the cosmetic treatment of Acne Vulgaris.
- 20 3. A method according to claim 1 or 2, wherein the illuminating radiation is of a predetermined wavelength.
- 25 4. A method according to any preceding claim, wherein the interactions (a) and (b) occur substantially contemporaneously.
- 30 5. A method according to any preceding claim, wherein the reaction leading to at least partial disabling or eradication of the cause of the skin condition is a photochemical reaction.

6. A method according to any preceding claim, wherein the illuminating radiation delivered is pulsed.
7. A method according to claim 6, wherein the pulse duration of the illuminating radiation is less than the thermal relaxation time of the target structure.
8. A method according to claim 6 or 7, wherein the pulse duration of the illuminating radiation is between  $10\mu\text{s}$  to 100ms.
9. A method according to claim 8, wherein the pulse duration of the illuminating radiation is between  $50\mu\text{s}$  to 10ms.
10. A method according to any preceding claim, wherein the wavelength of the illuminating radiation is in the range of 400nm to 1500nm.
11. A method according to any preceding claim, wherein the illuminating wavelength is in the range 500nm to 650nm.
12. A method according to any preceding claim, wherein the wavelength of the illuminating radiation comprises a primary wavelength or narrow wavelength band substantially in the range 570nm to 590nm.
13. A method according to any preceding claim, wherein the energy density of the illuminating radiation is in the range of  $0.5\text{J}/\text{cm}^2$  to  $5\text{J}/\text{cm}^2$ .

14. Apparatus for cosmetic treatment of a skin condition comprising illuminating radiation delivery means for delivering illuminating radiation to a target skin zone or structure.
- 5 15. Apparatus according to claim 14, for cosmetic treatment of Acne Vulgaris.
- 10 16. Apparatus according to claim 14 or 15, arranged to output radiation of a discrete wavelength or narrow primary wavelength band substantially in or about the range 400nm to 1500nm.
- 15 17. Apparatus according to claim 16, arranged to output radiation of a discrete wavelength or narrow primary wavelength band substantially in or about the range 500nm to 650nm.
- 20 18. Apparatus according to claim 17, arranged to output radiation of a discrete wavelength or narrow primary wavelength band substantially in or about the range 570nm to 595nm.
- 25 19. Apparatus according to any of claims 14 to 18, arranged to deliver radiation at an energy density at the skin surface substantially in the range 0.5J/cm<sup>2</sup> to 5J/cm<sup>2</sup>.
- 30 20. Apparatus according to claim 19, configured to inhibit output of energies substantially above the range 0.5J/cm<sup>2</sup> to 5J/cm<sup>2</sup>.

21. Apparatus according to claim 19 or 20, configured to permit variable selection of energy densities within the range  $0.5\text{J}/\text{cm}^2$  to  $5\text{J}/\text{cm}^2$ .
- 5 22. Apparatus according to any of claims 14 to 21, arranged to deliver illuminating radiation in a pulsed regime.
- 10 23. Apparatus according to claim 22, wherein the pulse duration of the illuminating radiation is substantially in the range  $10\mu\text{s}$  to  $100\text{ms}$ .
- 15 24. Apparatus according to claim 23, wherein the pulse duration of the illuminating radiation is substantially in the range  $50\mu\text{s}$  to  $10\text{ms}$ .
- 20 25. A method or apparatus for the manufacture of an agent for the treatment of a skin condition, the agent comprising illuminating radiation active to effect at the target zone the following interactions:
- (a) a reaction leading to at least partial disabling of the cause of the skin condition; and
  - (b) non-ablative heating of tissue stimulating an inflammatory response to a degree sufficient to
- 25 effect collagen production.
26. A method according to claim 25, for the treatment of Acne Vulgaris.



Application No: GB 0025639.6  
Claims searched: 1-26

Examiner: Stephen Quick  
Date of search: 1 October 2001

## Patents Act 1977 Search Report under Section 17

### Databases searched:

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

UK CI (Ed.S): A5R (REHR)

Int CI (Ed.7): A61N 5/06, 067

Other: Online: EPODOC, JAPIO, WPI

### Documents considered to be relevant:

Category	Identity of document and relevant passage	Relevant to claims
X,E	GB 2356570 A (WARBURTON ET AL) 30.05.2001, see whole document, especially page 1	1, 14 & 25 at least
X	GB 2336545 A (O-LYS), see whole document, especially page 1 (last paragraph), page 2 (2nd paragraph) and pages 4 & 5 (bridging paragraph)	1, 14 & 25 at least
X	GB 2272158 A (TANSUN), "sun tan" apparatus	14 at least
X	EP 0884066 A2 (SLI LICHT-SYSTEME) see whole document, especially page 1 (lines 3-4 & 10-20) and WPI Abstract Accession No 1999-026352/03	1, 14 & 25 at least
X	EP 0159446 A2 (LASERCARE), see page 2 lines 8-14	14 at least
X,E	WO 00/74782 A1 (SLS BIOPHILE) 14.12.2000, see whole document, especially paragraph bridging pages 1 & 2, page 6 (last complete paragraph) and page 8 (line 26)	14 & 25 at least
X	WO 00/32272 A1 (SLI LICHT-SYSTEME) see whole document, especially page 1 (paragraphs 1 & 4-7)	1, 14 & 25 at least

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
&	Member of the same patent family	E	Patent document published on or after, but with priority date earlier than, the filing date of this application.



INVESTOR IN PEOPLE

**Application No:** GB 0025639.6

**Claims searched:** 1-26

**Examiner:** Stephen Quick

**Date of search:** 1 October 2001

Category	Identity of document and relevant passage	Relevant to claims
X	WO 98/38933 A1 (NEW STAR LASERS), see whole document, especially pages 5 (last complete paragraph), 7 (lines 26-27), 9 (line 33) & 12 (lines 31-32), and reference to 660 nm light treatment of acne in US5549660 A	1, 14 & 25 at least
X	WO 96/33773 A2 (OLAVESEN), see whole document, especially page 1 (paragraphs 1-3)	1, 14 & 25 at least
X	US 5549660 A (AMRON), see whole document, especially columns 1 (lines 44-58) & 3 (lines 43-46)	14 at least

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
&	Member of the same patent family	E	Patent document published on or after, but with priority date earlier than, the filing date of this application.